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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,073	11/14/2001	David Botstein	P2730P1C15	4049

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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
12/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/991,073	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/2/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *122-126 and 129-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *122-126, 129-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/2/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/2/2007 has been entered.

Claims 122-126 and 129-131 are pending and under consideration. No claim has been amended.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 122-126 and 129-131 are rejected under §35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

This rejection is maintained for reasons of record at pages 3-5 of the Examiner's Answer mailed 4/10/2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 122-126 and 129-131 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

This rejection is maintained for reasons of record at pages 6-8 of the Examiner's Answer mailed 4/10/2006.

Applicants arguments filed 10/2/2007 are largely cumulative and duplicative of the arguments made in the Appeal Brief, and were fully responded to in the Examiner's answer, mailed 4/10/2006. A number of applicants arguments continue to be directed at the predictability of protein levels when *mRNA* levels are amplified. The Examiner maintains that the most significant issue in this case is that the data are drawn to *genomic* data, and *not* mRNA data. While the Examiner concedes that if *mRNA* levels were shown to be significantly higher in a significant proportion of a given tumor type that such would be indicative of utility for the claimed antibodies, she maintains that such is not predictable based upon the data in the specification, which are specifically drawn to amplification of *genomic* DNA.

With regard to arguments at page 8 of the response, applicants are referred to page 18 of the Examiner's answer.

At page 9, applicants argue that the Examiner is focusing on the mechanism rather than the positive result itself. This argument has been fully considered but is not deemed persuasive because it misconstrues the Examiner's position, which is that the result itself is not sufficient to establish that it is more likely than not that amplification of the portion of the chromosome that has the gene from which SEQ. ID NO. 223 is transcribed. *One* type of information that might, in combination with that result, indicate that one would expect the gene to be transcribed at higher level due to the amplification of the chromosomal DNA would be that the protein encoded thereby would confer an advantage to the cell, as supported by the cited art. While such

information is not required, it is an example of one type of additional information that would, in concert with the disclosed result, establish utility. However, such is not the case for PRO809.

Contrary to the argument at page 9, applicants have not provided an overwhelming amount of evidence that amplification of genomic DNA, on the order of that found for PRO809 (approximately two-fold) would be expected to correspond to a detectable increase in the encoded protein. These arguments have been addressed fully in the Examiner's Answer.

At page 10, applicants argue that Dr. Polakis' statements are based on factual, experimental finding, clearly set forth in the Declaration. This argument has been fully considered but is not deemed persuasive because as stated in the previous Office Action, . The fact that needs to be established here is that a ΔCt value of at least 1.0 would be predictive of increased protein expression. Applicants have never addressed this point directly, and the Polakis declarations do not address this point. With respect to the data in the second Polakis declaration, as stated in the previous Office Action, Dr. Polakis refers to facts; however, the data refer to the mRNA's in question only by UNQ numbers; UNQ464, which is PRO809, is not represented, and declarant provides no information about the sequences that *are* represented; the assertion in the specification is that PRO809 was found to be amplified approximately two fold in 3 of 10 human lung tumor squamous cell carcinoma cell lines, 2 of 9 human lung tumor adenocarcinoma cell lines, and the sole human lung tumor large cell carcinoma cell line. It is not clear whether any or all of these tissues were represented in the data. There is no indication of *how much* the mRNA and protein were overexpressed, as there is no actual description of the experiment that was done, but rather a conclusory statement as to what was measured, and what it means. The Examiner cannot determine that the facts presented lead to the declarant's conclusion; hence, the conclusion is afforded only the weight of opinion, which is contradicted by the cited art.

At page 10, applicants argue that the two Polakis declarations are not inconsistent, and "use the exact same wording". This argument has been fully considered but is not deemed persuasive because it is incorrect. As stated in the previous Office action, "In the first declaration, Dr. Polakis declares that "In approximately 80% of our observations we have found that increases in the level of a particular mRNA correlates with changes in the level of protein expressed from that mRNA when human tumor cells are compared with their corresponding

normal cells." In the second, he states that "of the 31 genes identified as being detectably overexpressed in human tumor tissue as compared to normal human tissue at the mRNA level, 28 of them (i.e. greater than 90%) are also detectably overexpressed in human tumor tissue as compared to normal human tissue at the protein level."

It cannot be determined whether the two declarations are referring to the same data set, or different data sets. Further, there has been no explanation of why the Declarant now refers to tumor *tissue* rather than tumor *cells,* nor what the perceived significance of this change is."

Applicants arguments to the contrary are not sufficient to allow re-interpretation of the declarations. The only person who can speak to what Dr. Polakis meant is Dr. Polakis himself. As no further declaration has been submitted, the Examiner maintains her position.

At page 11, applicants refer to a decision by the Board of Appeals and Interferences regarding the predictability of protein levels based upon mRNA. This argument has been fully considered but is not deemed persuasive because :

(a) The decision was rendered in application serial number 10/123212. Applicants filed the appeal brief in that case on 9/9/2005, and a Supplemental Appeal Brief on 3/17/2006. In the instant case, 09/991073, an appeal brief was filed 12/22/2005. While two related cases were identified in the appeal brief, 10/123212 was not, despite the fact that the appeal in that case had been filed three months earlier. Accordingly, applicants are estopped, and cannot now argue that the results of that appeal are pertinent to this case.

(b) Each case must be examined on its own merits.

(c) The issues in the two cases are substantively different; the issue in 10/123212 was predictability of protein based on *demonstrated* elevated mRNA levels. As repeatedly stated in the prosecution of this applications, that is *not* the issue here.

In closing, the Examiner notes that submission of *data* showing PRO809 protein or mRNA to be significantly overexpressed in a significant proportion of samples of any of the tested tumor types would be convincing evidence of utility. However, it remains that aneuploidy is one of the hallmarks of tumor formation, and that the specification as filed shows only levels of genomic amplification consistent with such, and that on the basis of such it is *not* predictable that the PRO809 protein would be overexpressed in the tested cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 122-126 and 129-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over clone H74302, isolated by L. Hillier et al., WashUMerck EST Project 1995 in view of Sibson et al., WO94/01548.

This rejection is maintained for reasons of record at pages 8-9 of the Examiner's Answer mailed 4/10/2006. Applicants argument that the clone of Hillier would not encode the same protein as their clone is not persuasive, as Hillier's clone is cited in the specification as the source of the nucleic acid. As stated in the First Office Action on the Merits,

"By applicants admission at page 454 of the specification, the clone that was sequenced and designated DNA57836-1338 or PRO809, was purchased from Merck under clone designation H74302. According to NCBI, the cDNA was double stranded, and inserted in the "Lafmid BA vector", which was propagated in E. coli cells. With respect to claim 136, the DNA would necessarily have been "operably linked" to sequences in the vector for control of replication of the vector."

It remains that the two sequences are one, and therefore cannot differ.

Applicants also argue that they have submitted a translation of the protein obtained by Hillier, and that it is 199 amino acids long. This argument has been fully considered but is not deemed persuasive because it is not clear from the submitted document what was translated, nor why there are so many "unknown" (X) residues in the sequences, nor how the translation can be

different from that obtained by applicants, given the admission in the specification that the DNA they used was Hillier's. Applicants further argue that alignment of the proteins encoded by the two sequences reveals an area of only 16 residues' identity. This argument has been fully considered but is not deemed persuasive because as stated above, applicants have not explained how a sequence can be different from itself. It remains that the specification admits to having bought Hillier's clone. Accordingly, arguments that the sequence is *different* from Hillier's clone cannot be found persuasive in the absence of an explanation as to why applicants sequence *could be* different from what was purchased (which explanation would likely be inconsistent with the specification as originally filed. Further, the "alignment" submitted does not show the sequences themselves, but rather only the alleged 16 residue overlap.

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Manjunath Rao, at telephone number 571-272-0939.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lorraine Spector/
Primary Examiner, Art Unit 1647